REMARKS

1. Introduction

In the Office Action mailed March 11, 2005, the Examiner rejected claims 1-4 and 8 under 35 U.S.C. 103(a) as being unpatentable over Dixon et al., U.S. Patent No. 4,835,100 ("Dixon") in view of Nasir et al., *Combinatorial Chemistry & High Throughput Screening* ("Nasir"). The Examiner rejected claims 5-7 under 35 U.S.C. 103(a) as being unpatentable over Dixon in view of Nasir and further in view of Michel et al., U.S. Patent No. 5,741,654 ("Michel"). The Examiner rejected claims 9-10 under 35 U.S.C. 103(a) as being unpatentable over Dixon in view of Nasir and further in view of McMahon et al., U.S. Patent No. 5,166,078 ("McMahon"). The Examiner rejected claims 11-18 as being unpatentable over Nasir in view of Dixon.

For the reasons set forth below, Applicants respectfully request reconsideration and allowance of the claims.

2. Response to Claim Rejections

The Examiner's claim rejections are all based on combining the teachings of Dixon and Nasir. However, the Dixon/Nasir combination does not teach the claimed subject matter. In addition, the Examiner has not shown that the prior art taught a reasonable expectation of success. These two points are described in detail below.

a. Dixon and Nasir Do Not Teach The Claimed Subject Matter

The Examiner has alleged that Dixon teaches converting aflatoxin B1 to aflatoxin B1-oxime for labeling (col. 4, line 62 – col. 5, line 15). In fact, Dixon does not state that the conversion of aflatoxin to aflatoxin oxime was for purposes of **labeling**. Instead, Dixon teaches

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converting aflatoxin B_1 into aflatoxin B_1-oxime in order to (i) conjugate bovine serum albumin (BSA) for use as an immunogen and (ii) conjugate ovalbumin (OA) for use as a solid phase antigen in competitive indirect ELISA (col. 4, lines 62-66). Thus, the BSA and OA are not labels.

Dixon also teaches using aflatoxin B_1 conjugated to an enzyme label, horseradish peroxidase (HRP), in a competitive direct ELISA assay (col. 6, lines 34-39). However, Dixon does not state that the aflatoxin B_1 was in the form of an oxime in the aflatoxin B_1-HRP conjugate. Instead, Dixon simply refers to "aflatoxin B_1 conjugated to horseradish peroxidase." The plain meaning of this statement is that aflatoxin B_1 itself was used, not aflatoxin B_1 oxime. This reading is reinforced by the fact that Dixon's discussion of converting aflatoxin B_1 to aflatoxin B_1 oxime makes no mention of conjugation to HRP (col. 4, line 62 – col. 5, line 15).

Accordingly, the Examiner's assertion that Dixon teaches converting aflatoxin to aflatoxin oxime for labeling is unsupported. For this reason alone, the Examiner's claim rejections are fatally flawed and should be withdrawn.

Even if it were to be assumed that Dixon somehow teaches conversion of aflatoxin to aflatoxin oxime for labeling, Nasir teaches away from labeling aflatoxin oxime with a fluorophore. In particular, Nasir teaches forming a tracer for a fluorescence polarization assay by conjugating a fluorophore to a mycotoxin antigen, not to a derivative of a mycotoxin antigen: "A mycotoxin antigen of interest is labeled with a suitable fluorescent molecule (tracer)." (Nasir, p. 182, col. 1). Because Nasir teaches away from using aflatoxin oxime, Nasir cannot be combined with Dixon to establish a *prima facie* case of obviousness. *See* MPEP § 2146(X)(D)(2) ("It is improper to combine references where the references teach away from their combination.").

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Accordingly, the Examiner has failed to establish that Dixon and Nasir can be combined to teach the claimed subject matter and, thus, has failed to establish a *prima facie* case of obviousness.

c. No Prior Art Teaching Of A Reasonable Expectation Of Success

In order to establish a *prima facie* case of obviousness, the Examiner must also show that the prior art taught a reasonable expectation of success. *See* MPEP § 2143. In this case, the claims specify that the tracer (aflatoxin oxime conjugated to a fluorophore) has the special property of being able to bind to an antibody specific for aflatoxin "to produce a detectable change in fluorescence polarization." However, the Examiner has not shown that the prior art teaches a reasonable expectation of success with respect to achieving this special property.

As noted above, the Nasir reference teaches labeling the mycotoxin antigen with a fluorescent molecule. However, if a derivative of a mycotoxin antigen is fluorescently labeled instead, e.g., an aflatoxin oxime conjugated to a fluorophore, where is the prior art teaching that the product would have the special property of being able to bind to an antibody to produce a detectable change in fluorescence polarization?

The Examiner has failed to identify any such teaching in the prior art. Instead, the Examiner has relied on a supposed teaching in Dixon of equivalence between "fluorophore labels" and "BSA labels." As an initial matter, Dixon does not refer to "BSA labels" at all. Instead, Dixon teaches the conjugation of aflatoxin oxime to BSA for use as an immunogen (col. 4, lines 62-64). In particular, Dixon discloses that aflatoxin B_1-BSA was injected into mice to produce antibodies that were then screened for sensitivity (col. 5, lines 16-31, lines 61-68). Thus, Dixon teaches using BSA as an immunogen, not as a label.

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In any event, the section in Dixon that the Examiner cited as supposedly teaching equivalence between different types of labels simply teaches the advantages of monoclonal antibodies:

> It would be advantageous to use monoclonal antibodies for conducting the immunoassays for aflatoxin B_1 and G_1. Hybridomas produce unlimited amounts of highly uniform monoclonal antibodies. The monoclonal antibodies can then be used in the development of a colorimetric commercial assay systems for the mycotoxins, such as Enzyme Linked Immunosorbent Assay (ELISA) or fluorescent antibody tests.

(col. 2, lines 22-29). The mere fact that monoclonal antibodies can be used to develop both ELISA and fluorescent antibody tests does not make the two tests equivalent, nor does it make the different types of labels used in the tests equivalent:

> In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents.

MPEP § 2144.06. Thus, even if the Examiner's statement that "fluorophore labels versus BSA labels are equal equivalents because both are used for detections purposes and are reacted with their respective antibodies" were accurate (as noted above, Dixon teaches using BSA as an immunogen, not as a label), it is not a rationale that can support an obviousness rejection. In fact, Nasir teaches that heterogeneous assays, e.g., ELISA assays, and homogeneous assays, e.g., fluorescent polarization assays, can have different characteristics:

> In ELISA compounds adsorbed to the solid phase may have different affinities than in solution. The adsorbed antigens may denature with time [29], and at the solid phase steric hindrance might occur for larger molecules [30].

(Nasir, p. 191, col. 2). Thus, the prior art teaches away from any asserted equivalence between ELISA and fluorescence polarization assays.

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Finally, Dixon's reference to "fluorescent antibody tests" in no way suggests the fluorescence polarization assays and kits claimed in the present application. In a fluorescent antibody test, the **antibody** is labeled with a fluorophore. In contrast, the pending claims recite a tracer comprising an **aflatoxin oxime** conjugated to a fluorophore. Another important difference is that fluorescence polarization is not necessarily measured in a fluorescent antibody test; instead detection could be based on the mere presence of fluorescence. In contrast, the pending claims recite that the tracer is able to bind to an antibody to produce a detectable change in fluorescence polarization. Nothing in Dixon teaches a tracer that has this special property.

Accordingly, the Examiner has failed to identify a prior art teaching of a reasonable expectation of success and has failed to establish a *prima facie* case of obviousness.

3. Conclusion

Applicants submit that the present application is in condition for allowance and notice to that effect is hereby requested. Should the Examiner feel that further dialog would advance the subject application to issuance, the Examiner is invited to telephone the undersigned at any time at (312) 913-0001.

Respectfully submitted,

Date: May 25, 2005

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